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Preparation, characterization and evaluation of finasteride ethosomes

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Abstract

The present investigation attempted to prepare and evaluate the finasteride ethosomes for transdermal drug delivery. The ethosomal formulations were developed using different concentrations of ethanol (20-60%) and soya lecithin (1-5%). *In-vitro* release studies of formulation containing 30% ethanol and 3% soya lecithin showed highest % drug release (82.66%) with highest transdermal flux. The entrapment efficiency and drug content of optimized formulation were found to be 85.32% and 99.5% respectively. Scanning Electron micrographs revealed that the formed vesicles were spherical in shape with uniform size. It was also observed that concentration of the ethanol had profound influence on entrapment efficiency. The drug release from the formed vesicles was found to follow first order kinetics with higuchi diffusion mechanism. The transdermal delivery of finasteride could be potentially enhanced when they were formulated into ethosomes. This ethosomal drug delivery was found to be promising than could be a nanogel.

Keywords: Finasteride, ethosomes, Scanning electron microscopy, transdermal delivery, Zeta potential.

Introduction

Transdermal drug delivery system (TDDS) showed promising result in comparison to oral drug delivery system as it eliminates gastrointestinal involvement and first pass metabolism of the drug. The skin acts as a major target as well as a principle barrier for topical/ transdermal drug delivery. Stratum corneum (SC) permits only the lipophilic drugs having molecular weight < 500 daltons [1] and acts as a barrier. Many approaches have been attempted to overcome this property of skin, includes the use of chemical enhancers like surfactants, organic solvents, physical enhancers such as iontophoresis, sonophoresis, microneedles, electroporation etc. and various methods have been assessed to increase permeation and amongst them the best is lipid vesicles can modulate barrier property of SC [2,3]. Vesicles act as carrier systems, able to transport large molecular weight drugs into the skin or even into the systemic circulation [4].

Conventional liposomes have been generally reported as carriers of drugs with minimal diffusion into deeper tissues, due to their large size and lack of flexibility [5,6]. After meticulous research over the decades led to the development of a new class of lipid vesicles that are shows ultra-elastic property and were considered as ethosomes. Touitou *et al*., (1998) discovered lipid vesicular systems embedding ethanol in relatively with higher concentration [7]. Ethosomes are novel lipid carriers comprised ethanol, phospholipid, bile salts, surfactants and water [8]. These were show augmented permeation through the skin due to the escalated fluidity of SC lipids [9,10]. Further, due high flexibility of ethosomal membranes by excess ethanol, these are squeezed into the skin their self through pores, became much smaller than their actual size. Ethosomes are soft, flexible vesicles and considerable dosage forms can efficiently load higher quantities of drug, permeate in depth to the skin than conventional liposomes [11-13].

Finasteride is a type-II 5α-reductase inhibitor, *N*-(1,1-dimethylethyl)-3-oxo-4-aza-5α-androst-1-ene, (5α, 17β) carboxamide [14] and is used in the treatment of androgenic alopecia and as surgical alternative for benign prostatic hyperplasia. The oral bioavailability of finasteride is 65%, mean half-life is 4.5 h and 8h in men 18-60 and 70 years of age respectively. In this study, transdermal drug delivery system of ethosomes was designed and developed with finasteride. Effects of various excipients on the incompatibility, entrapment efficiency, drug release, percutaneous absorption, stability studies were evaluated. Characterization of ethosomes was performed by using SEM, micorscopic examination, zetapotential and size distribution. Physical properties of ethosomal gel were evaluated such as organoleptic characters, washability, spreadability, viscosity, pH and drug content uniformity. Further,

studied skin irritation test, in-vitro drug release by dialysis membrane and correlated with ex-vivo drug release on rat skin.

Materials and Methods

Finasteride was obtained as a gift sample from Aurobindo Phama Ltd., Hyderabad, India. propylene glycol, L-soya lecithin, carbopol-934, cholesterol, ethanol and triethanol amine were procured from SD fine chem. Ltd., Mumbai, India. Other chemicals and reagents used were of analytical grade.

Analysis of Finasteride drug in vesicles

Calibration curve was constructed using UV Spectrophotometer in the concentration range of 5-25 µg/mL for Finasteride and plotted a linear curve between absorbance vs. concentration (µg/mL) at 254 nm (Figure. 1).

Compatibility Studies

IR spectroscopy was used to investigate interactions between different components in the formulation. One part of the sample and three parts of potassium bromide were taken in a mortar and triturated well. A small amount of triturated sample was taken into a pellet maker and was compressed at 10 kg/cm2 using hydraulic press (Bruker). The pellet was kept on to the sample holder and scanned from 400 to 4000 cm-1 in IR spectrophotometer. The spectrum obtained was compared with original spectra of drug and optimized formulation.

Preparation of finasteride loaded ethosomes and ethosomal gel

The ethosomes loaded with finasteride were prepared by the cold method followed by ultra-sonication according to Touitou et al., (1999) [12]. In brief, phospholipid (L-soya lecithin), cholesterol and the drug were blended and dissolved in ethanol in a covered vessel with vigorous stirring at 700 rpm at room temperature. Propylene glycol was added at 40°C mixed; later water was added and whole mixture was stirred for 5 min in a covered vessel. Size reduction was done by sonication and the suspension was stored in refrigerator. The composition of ethosomal formulations of finasteride were tabulated in table 1. The ethosomal vesicles suspension was incorporated into carbopol gel 934 (1%, 1.5%, 2% w/w) slowly to ultrapure water and kept for 20 min. Triethanolamine was added to it drop wise and pH was adjusted to 7.4. The composition of ethosomal gel was given in table 2.

Table 1. Composition of various ethosomal formulations of finesteride drug

Formulation Code	Finasteride (mg)	L-Soya lecithin (%)	Cholesterol (mg)	Ethanol (%)	Propylene glycol (%)	Water (mL)
F_1	5	2	5	20	10	Q.S
F_2	5	2.5	5	20	10	Q.S
F_3	5	3	5	20	10	Q.S
F_4	5	3.5	5	20	10	Q.S
F_5	5	4	5	20	10	Q.S
F_6	5	4.5	5	20	10	Q.S
F_7	5	5	5	20	10	Q.S
F_8	5	5.5	5	20	10	Q.S
F_9	5	6	5	20	10	Q.S
F_{10}	5	3	5	30	10	Q.S
F_{11}	5	3	5	30	15	Q.S
F_{12}	5	3	5	30	20	Q.S
F_{13}	5	3	5	30	25	Q.S
F_{14}	5	3	5	30	30	Q.S
F_{15}	5	3	5	40	20	Q.S
F_{16}	5	3	5	50	20	Q.S
F_{17}	5	3	5	60	20	Q.S
F_{18}	5	3	5	20	20	Q.S
F_{19}	5	3	10	30	20	Q.S
F_{20}	5	3	---	30	20	Q.S
F_{11a} (F.S)	5	---	---	---	---	Q.S
F_{11b}^*	5	---	5	30	---	Q.S

F.S= Free Suspension, F_{11}^* = Effect of stabilizer on optimized formula.

Entrapment Efficiency

The amount of finasteride encapsulated per unit weight of the ethosomes was determined after separation of the free drug and solid lipids from the aqueous medium. Ultracentrifugation was performed at 4°C, at 40,000 rpm for 3 h (Touitou et al., 1998) [7] and suspension was assayed both in the sediment and in the supernatant. The entrapment efficiency was calculated from the relationship:

$$EE = \frac{T - C}{T} \times 100 \quad (1)$$

Where, T is the total amount of drug that is detected both in the supernatant and sediment, C is the amount of drug detected only in the supernatant.

Table 2. Composition of different ethosomal gel formulations

Formulation	Carbopol D 934 (%)	Ethosomal Suspension (ml)	Triethanol amine (ml)	Water
F_{11a}	1	20	0.05	Q.S
F_{11b}	1.5	20	0.05	Q.S
F_{11c}	2	20	0.05	Q.S
F_{11b^*}	1.5	Free Drug (0.005g)	0.05	Q.S

F_{11b^*}= Free drug gel.

Characterization of Ethosomes

Microscopic Examination of Particle Size and Shape

Microscopic analysis was performed to determine the average size of ethosomes [7]. A sample of ethosomes was suitably diluted with distilled water in order to observe individual vesicle and a drop of diluted suspension was put on a glass slide covered with cover slip and examined under microscope (magnification 15 × 45 X). All measurements were performed in triplicates and the formed vesicles were spherical in shape.

Scanning Electron Microscopic Studies

The ethosomal dispersion was diluted appropriately and sonicated. Few drops of the dispersion were placed on the grid and allowed to dry [15]. After the samples were dried thoroughly, the Images were recorded on a scanning electron micrograph (magnification: 60x, accelerating voltage: 12.0kV and at 25±2°C).

Zeta Potential Analysis

Zeta potential is the measure of the magnitude of the electrostatic or the charge repulsion or attraction between particles. The zeta potential was determined using zeta potential analyzer (nano-particle analyzer SZ-100) at 25°C. Electrophoretic mobility and mean zeta potential values were obtained directly from the measurement.

Size Distribution

The size of ethosomes ranges between tens of nanometers to microns and is influenced by the composition of the formulation. Particle size of vesicle can be determined by dynamic light scattering (DLS) and also can be characterized by light microscopy with an eyepiece micrometer which is calibrated with a stage micrometer. The diameters of 150 vesicles were determined randomly using calibrated eyepiece micrometer with stage micrometer. The average diameter was calculated using the formula [16].

$$\text{Average diameter} = \frac{Snd}{Sn} \quad (2)$$

Where; n = number of vesicles, d = diameter of vesicles

Characterization and Evaluation of Ethosomal Gel

Determination of Organoleptic Characters, Washability and Spreadability

The formulations were tested for their organoleptic properties like color, odor, texture, phase separation and feel upon application (grittiness, greasiness). Washability of the gel was determined by a small quantity of gel was applied on the skin. After washing with water it is checked for whether the gel was completely washed out or not. Spreadability was determined by using modified wooden block and glass slide apparatus. A measured amount of gel (0.5 g) was placed on fixed glass slide with a circle of 1cm diameter; the movable pan with a glass slide attached to it and was placed over the fixed glass slide, such that the gel was sandwiched between the two glass slides for 5min. The increase in the diameter due to spreading of the gel was noted and spreadability was determined using the formula.

$$S = \frac{M}{T} \quad (3)$$

Where, S is the Spreadability in g/s, M is the mass in grams and T is the time in seconds. The viscosity of ethosomal gel was determined by brook field viscometer with T-bar spindle (Sindle C, S-96). The spindle was rotated at 50rpm and recorded the readings after 30 sec.

pH, Percentage Drug Content and Content drug Uniformity

Solution of 1g of gel dissolved in 30mL of distilled water was prepared and pH was determined by using digital pH meter (Systronics 361) and the results were summarized in the table 3. The drug Content Uniformity [17] was determined 1g of gel was dissolved in a 100 mL of phosphate buffer pH 7.4 for 48 h with constant stirring using magnetic stirrer. Samples were taken from three different parts of the total ethosomal gel of 1g. Solution was then filtered and recorded the absorbance with UV-spectrophotometer at λ_{max} 254nm.

Skin irritation test

The developed formulations were tested for primary skin irritation on rats (male Wistar rats). The rats were taken and the abdominal skin of the rat was clipped free of hair 24 h prior to the formulation application. 0.5 g of each formulation was applied on the hair-free skin of rat by uniform spreading over an area of 4 cm^2. The skin surface was observed for visible changes such as erythema after 24, 48 and 72 h of the formulation application. The mean erythemal scores were recorded depending on the degree of erythema: no erythema = 0, slight erythema (barely perceptible- light pink) = 1, moderate erythema (dark pink) = 2, moderate to severe erythema (light red) = 3 and severe erythema (extreme redness) = 4.

Stability studies

Stability study was carried out for finasteride ethosomal preparation by using stability chamber (Thermo lab, India-standard) at two different temperatures i.e. refrigeration temperature (4±2°C) and at room temperature (27±2°C) for 9 weeks. The formulations subjected for stability were stored in borosilicate container and were analyzed for any physical changes such as color and appearance, for any chemical changes such as the In-vitro percentage drug release [18].

Drug release studies

In-vitro release kinetics by using dialysis membrane

In-vitro drug release studies were performed using a modified Franz diffusion cell. The membrane was soaked in double distilled water for 12 h before mounting on a Franz diffusion cell [19]. The effective permeation area of the diffusion cell and receptor cell volume was 2.4 cm and 200 mL respectively. The temperature was maintained at 37±0.5°C. The receptor compartment contained 200 mL of pH 7.4 buffer and was constantly stirred by magnetic stirrer at 800 rpm. Prepared dialysis membrane was mounted between the donor and the receptor compartments. The optimized ethosomal gel (0.5 g) was applied to the dialysis membrane and the content of diffusion cell was kept under constant stirring then 5 mL of samples were (replenished with equal volume of fresh pH 7.4 buffer) withdrawn from receptor compartment of diffusion cell at predetermined time intervals and analyzed by spectrophotometric method at 254 nm after suitable dilution. The in-vitro data was fitted into various kinetic models i.e. zero order, first order, Higuchi, Korsmeyer-Peppa's models.

Ex-vivo Drug Diffusion Study Using Rat Skin

Skin permeation of finasteride ethosomal gel was studied using freshly excised hairless abdominal skin of a male wistar rat (250 g, 8 weeks), which was housed individually in the animal house with food and water. The rat was sacrificed by decapitation. Then, the hairs in the abdominal area of the animal were carefully cut as short as possible with scissors. The skin was surgically removed, cleaned of muscle, fat and vasculature, and kept at –4°C for 24 h before the experiment. Skin samples were mounted on a modified franz diffusion cell (A = 0.785 cm^2) with the dermal skin surface exposed to the receiver phase and the stratum corneum remained in contact with the donor compartment.

Results and Discussion

Analysis of Finasteride drug in vesicles

Calibration graph was constructed for Finasteride by plotting absorbance *vs.* concentration (µg/mL) at 254 nm (Figure. 1). Correlation coefficient (r^2) was calculated in order to find the degree of linear relationship and was found to be 0.998. A mathematical form of linear relationship was obtained as y = 0.021x + 0.004 between the two variables i.e. absorbance *vs* concentration.

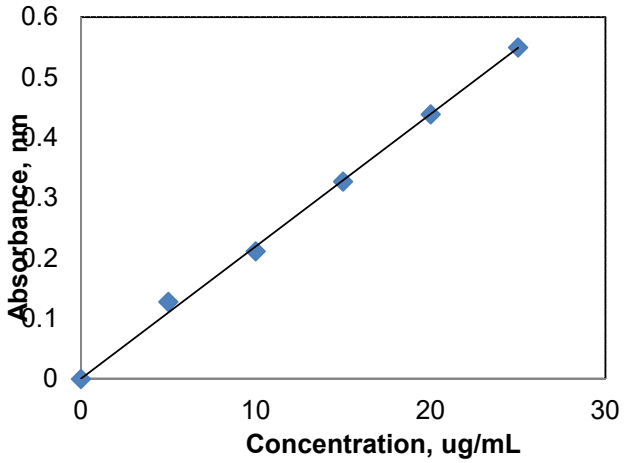

Figure. 1. Calibration curve of Finasteride at 254 nm

FTIR Studies

IR spectra was compared and checked for any shifting in functional peaks and non-involvement of functional group. The sharp peaks at 3428.45 and 3242.39 cm-1 designated as –N–H stretches of pure drug and slightly shifted to 3431.56 and 3243.52 cm-1 respectively which are not showing considerable changes. The peaks at 2849.26 and 815.48 cm-1 noted as –C–H bending and stretching respectively, no changes were observed. Further, a peak at 1687.75 cm-1 due to –C=O and there is no change after formulating of finasteride ethosomal gel. The other peaks appeared after formulation due to the excipients added. From the spectra various peaks of drug, physical mixture of drug and excipients studied, it is clear that there is no interaction between the selected carriers, drug and mixtures (Figure. 2).

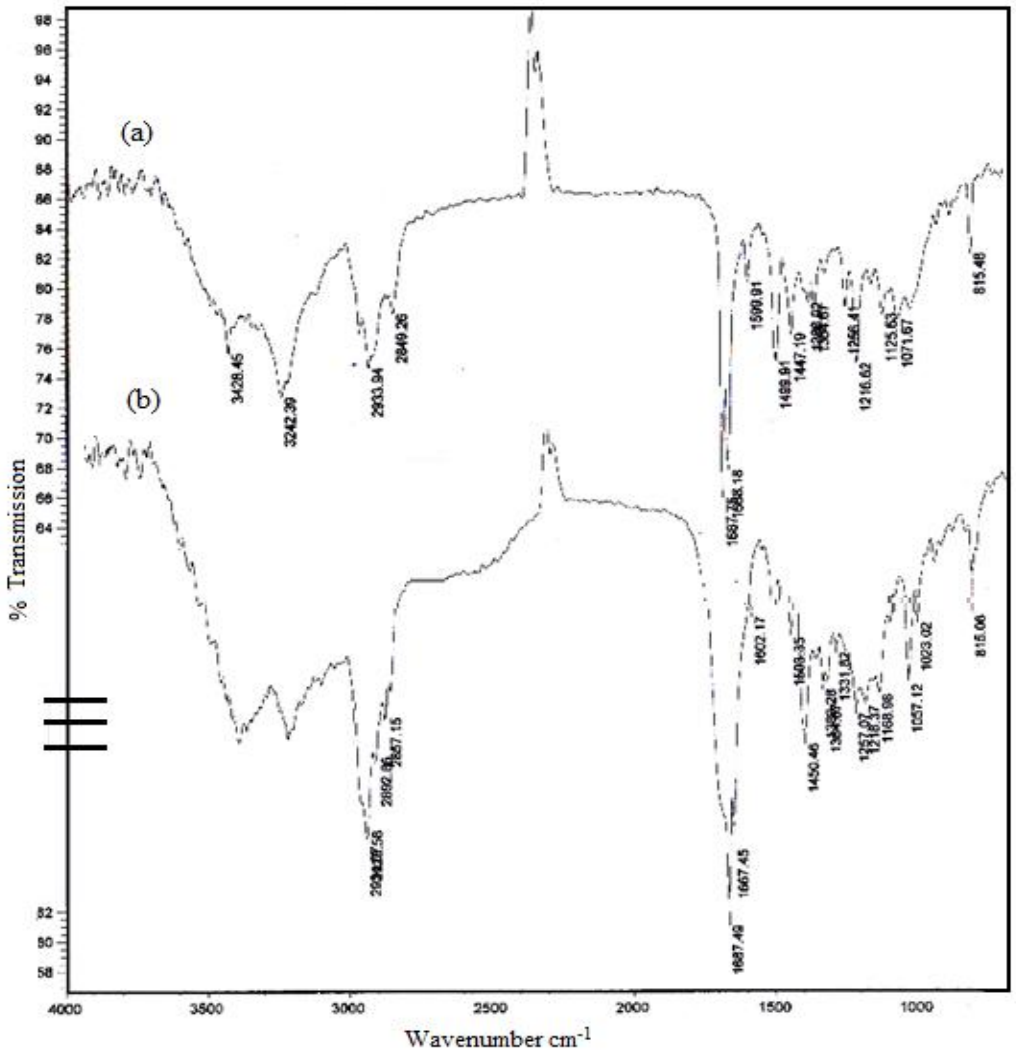

Figure. 2. FTIR Spectra of (a) pure finasteride drug (b) final optimized ethosomal gel

Entrapment Efficiency

For all formulations drug content, entrapment efficiency and pH were determined and were tabulated in table 3. The maximum entrapment efficiency of ethosomal vesicles was 85.32% for ethosomal formulation containing 30% ethanol which was almost double to the formulation containing 60% ethanol (F11). As the ethanol concentration increased from 20% to 60% w/w, there was increase in the entrapment efficiency and with further increase in the ethanol concentration (>30% w/w) the vesicle membrane becomes more permeable that lead to decrease in the entrapment efficiency. Results of entrapment efficiency also suggest that 3% phospholipid is optimal concentration for entrapment efficiency [20] and increased or decreased in concentration of phospholipid reduces the entrapment efficiency of vesicles (table 3).

Table 3. Drug entrapment efficiency, % Drug content and pH of Finasteride Ethosomal Gels

Formulation code	Entrapment Efficiency (%)	% Drug Content	pH
F_1	70.25±1.86	98.2±2.04	6.81±0.02
F_2	75.31±1.98	98.2±1.99	6.83±0.03
F_3	82.56±1.96	98.7±2.03	6.84±0.01
F_4	80.31±2.12	98.8±1.76	6.83±0.04
F_5	76.45±2.03	98.5±2.46	6.83±0.05
F_6	73.61±0.98	98.4±2.62	6.84±0.02
F_7	70.81±1.68	98.9±2.24	6.87±0.04
F_8	67.22±1.72	99.5±2.08	6.88±0.05
F_9	64.35±1.64	99.6±1.82	6.84±0.04
F_{10}	83.21±1.96	99.7±1.08	6.83±003
F_{11}	85.32±1.08	99.5±2.04	6.84±0.01
F_{12}	82.82±1.82	99.4±2.12	6.85±0.04
F_{13}	82.35±1.76	99.6±2.22	6.87±0.05
F_{14}	82.01±1.98	98.9±1.92	6.86±0.04
F_{15}	66.31±2.04	98.7±2.23	6.87±0.06
F_{16}	60.09±1.87	98.5±1.93	6.88±0.02
F_{17}	52.31±2.03	98.8±2.42	6.88±0.04
F_{18}	81.62±1.86	99.1±2.34	6.89±0.06
F_{19}	81.89±1.95	99.1±2.28	6.83±0.07
F_{20}	82.32±2.23	98.9±2.14	6.84±0.05

Characterization of finasteride ethosomal gel

Scanning Electron Microscopy (SEM)

The micrographs of the F11 illustrated spherical droplets in the nanometer range (Figure. 3).The results indicated that the particles were spherical and no drug crystals of particles were visible. The figure shows agglomeration of particles due to lipid nature of the carriers and sample preparation prior to SEM analysis. Some particle shapes deviating from sphericity might be due to the lipid modification during process of sample treatment. In addition the particle shape depends on the purity of the lipid.

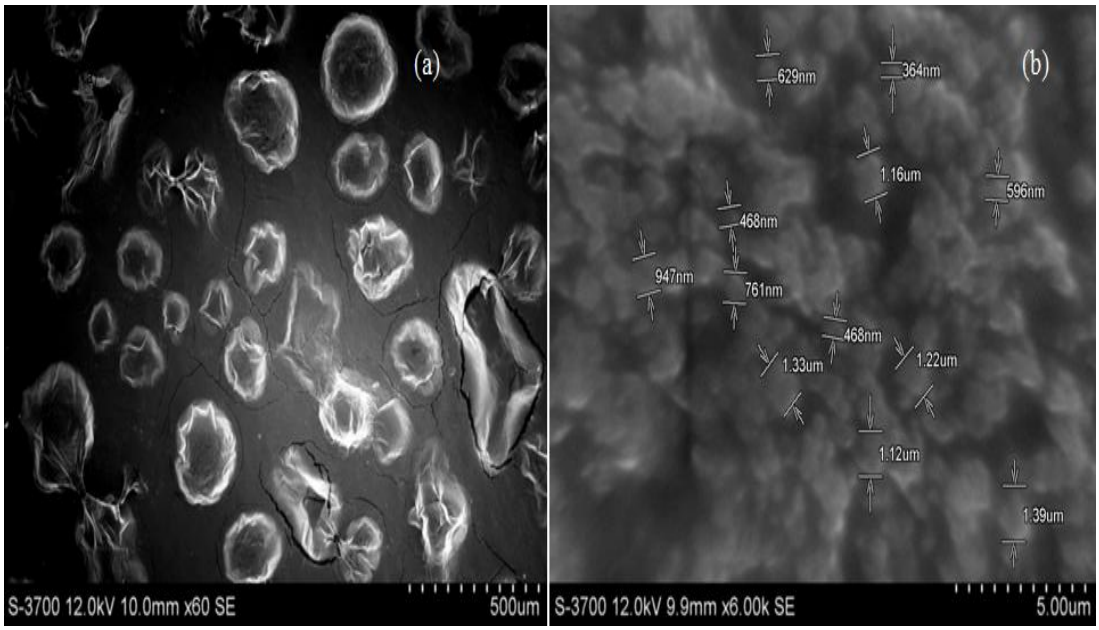

Figure. (3). Scanning Electron Microscopy micrograph (a) shape (b) size

Zeta Potential Analysis

To determine the long-term physical stability of the colloidal systems, the zeta potential was evaluated. The ethosomal dispersion of the optimized formula had higher zeta potential value, indicating the better stability. This resulted from electrostatic repulsion, which could prevent the bio-colloids from aggregation of nanoparticles of suspension. Zeta potential values higher than -30 mV show good physical stability [13], being optimized when they reach approximately -60 mV, exhibiting a very good physical stability during the shelf-life. In this study zeta potential of the F11 was found to be -37.9 mV demonstrating (Fig. 4a) that F11 possess a good physical stability since particle aggregation is not likely to occur owing to electrostatic repulsion. The similar results were reported by dubey et al., (2007) [13] for transdermal delivery of anti-psoriatic agent for ethosomes.

Size Distribution of Finasteride Ethosomal Formulations

The size of ethosomes decreased as the concentration of ethanol increased with the largest vesicles size 8.41 nm containing 30% ethanol (Fig. 4b). Results obtained in the present investigation are in conformity with the results of Touitou et al., (2000) [9]. As the phospholipid concentration increases the vesicle size also increases and by the increase in ethanol concentration the vesicle size also increases, so F11 was found to have an optimum average diameter of 8.28 nm.

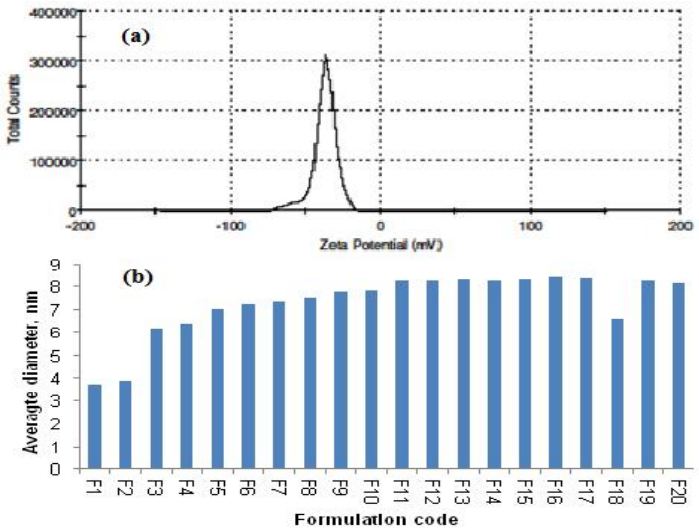

Figure. (4). Zeta potential (a) and Size distribution (b) of optimized ethosomal formulations

In-vitro Drug Release Study from Dialysis Membrane

In-vitro release studies by using vertical franz diffusion cell was performed for all the formulations at 37°C. A graph of % cumulative drug release vs time was plotted in figure 5.

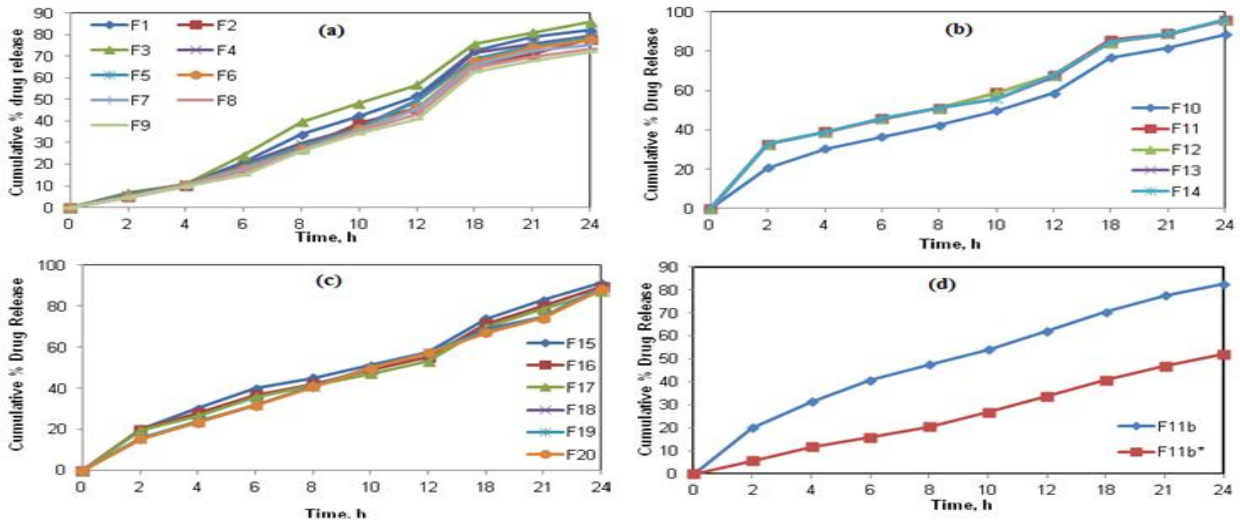

Figure. 5. In-vitro Drug Release Profile of formulations containing (a) 20% Ethanol (F1-F9), (b) 30% Ethanol (F10-F14), (c) 40, 50 and 60 % Ethanol (F15-F20) and (d) F_{11b} and F_{11b^*}.

Kinetics of Optimized Ethosomal Gel

The comparison of the optimized gel of F11b ethosomal suspension and F11b* gel containing Free drug was determined. After calculating and plotting the release kinetics for the optimized formulation of the ethosomal gel i.e. F11b and comparing this with the free drug gel formulation F11b*, it was found that the in-vitro drug release can be best explained by first order kinetics, as the plots showed highest linearity with regression coefficient R2 0.9933 (Figure. 6). The observations and kinetic model graphs showed that the mechanism of drug release was anomalous non-fickian diffusion for which n=0.56, followed by higuchi kinetics where ethosomes acts as reservoir system for continuous delivery of the drug (Table 4). The similar results were reported by Ying et al., (2013) for curcumin ethosomes delivery through skin [21].

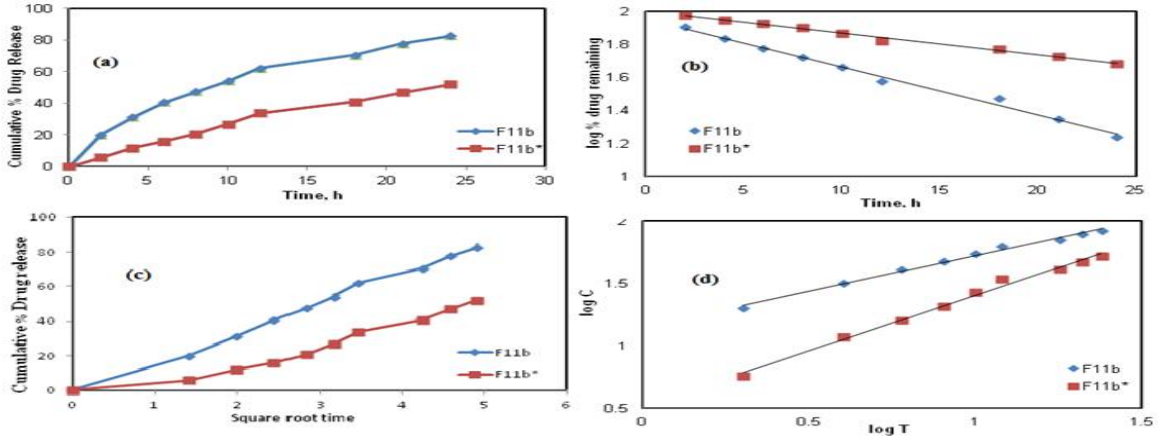

Fig. (6). Drug Release kinetics of optimized F_{11b} ethosomal gel (a) Zero Order Kinetics, (b) First Order Kinetics, (c) Higuchi Plot and (d) Korsmeyer-Peppas Plot

Table 4. Regression (R^2) values of pharmacokinetic profiles of optimized formulation

Formulation code	Zero order	First order	Higuchi	Korsmeyer-Peppas
F_{11b}	0.911	0.9933	0.995	0.9919

Ex-vivo drug diffusion through rat skin

After carrying out the in-vitro diffusion studies for all the formulations, the best formulation was F11 (30% ethanol and 3% soya lecithin). As rat skin showed good correlation with the in-vitro drug release of formulation F11, skin permeation studies of F11b was compared with the ex-vivo studies of F11b* which is a plain hydroalcoholic gel (fig. 7). This behaviour probably depended on the increase of the volume of the hydro-alcoholic compartment of ethosomes. The similar results were obtained in case paclitaxel loaded ethosomes reported by Donatella et al., (2012) [20].

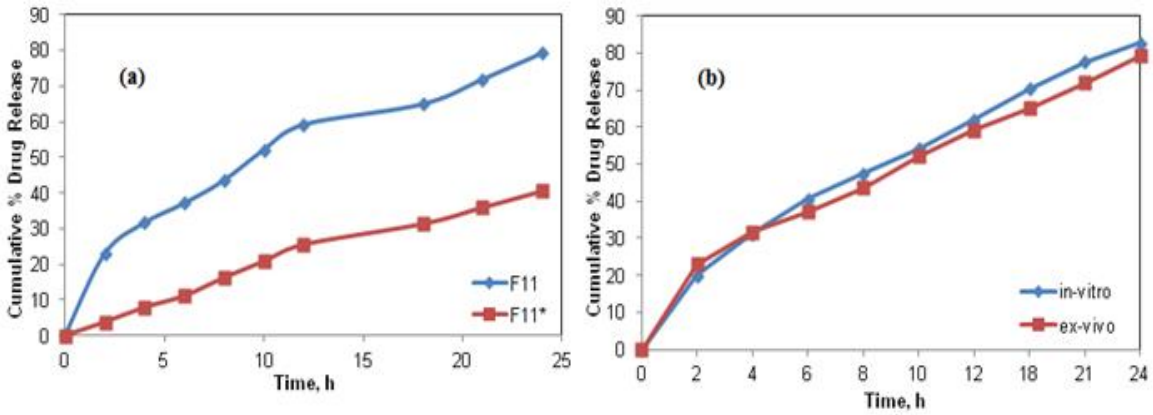

Figure. (7). Ex-vivo permeation studies (a) of optimized formulation using rat skin (b) and In-vitro and ex-vivo correlation**.**

Characterization and Evaluation of Ethosomal Gel

Determination of Organoleptic Characters, Washability and Spreadability

The organoleptic characters were determined and the color was found to be Golden yellow without any greasiness and grittiness. It was found that the ethosomal gel prepared can be applied easily, smoothly and there was no any skin irritation. The washability test was performed and it was found that the applied ethosomes were easily washable without leaving any residue on the surface of the skin. The Spreadability of the ethosomal gel was also very promise. The carbopol concentration of 1.5% was found to be optimum with 6.25 g. cm/sec, because the less carbopol concentration of 1% proved to have less consistency and was unable to apply properly. The more carbopol concentration of 2% was found to be more viscous and sticky in nature. The similar trend was shown by Sujitha et al., (2014) on piroxicam loaded ethosomes [22].

Determination of pH, Percentage Drug Content, viscosity and Content Uniformity

The pH of all ethosomal gels was found between 6.0 and 7.0 (Table 3) that lie in the normal pH range of skin, 4.0-6.8 and hence the preparations will be irritation free [22]. The pH of all the ethosomal gels was more or less equal to the skin pH, making the formulations suitable for application on skin aiding in systemic action. % Drug content of all the formulations was determined and was found to have a range of 98-100%. This shows that the drug was dispersed homogenously throughout the gels. The drug content for F13 formulation was found to be higher because of the optimum ethanol concentration. This shows that drug was dispersed homogenously throughout the gels. The Viscosity is optimum for 1.5% carbopol concentration since it has good flow and consistency unlike the 1% and the 2%, these both have either less or more viscosity compared to the optimum 1.5% carbopol. Viscosity of the optimized gel was found to have a range of 754-1350cp. The same trend was observed by Li et al., (2014) on the viscosity of apigenin ethosomes formulation [23].

Stability studies

After 9 weeks there was no change in appearance in ethosomal formulations throughout the period of study. Since the stability of drug and stability of vesicles are the major determinant for the stability of formulation, studies were carried to evaluate total drug content at room temperature (27±2°C) and refrigeration temperature (4±2°C) after 9 weeks (Table 5). Stability study could not be carried out at higher temperature (>room temperature) because phospholipid was used as the component for ethosomes and gets deteriorated at higher temperature. Loss in percentage of drug was not more than 4 percent. Highest drug loss was observed at room temperature after 9 weeks as compared to refrigeration temperature. Further Ketul et al., (2012) supported by reporting ethosomal gel for lipinavir drug [24].

Table 5. Loss in percentage drug release during stability studies of the optimized batch of Ethosomal Gel (F_{11b}).

Formulation code (F_{11b})		Percentage of drug release	Loss in percentage
Initial	4±2° C	82.66±1.26	0
	27±2° C	82.66±1.42	0
After 2 weeks	4±2° C	82.39±1.38	0.326±0.04
	27±2° C	82.25±1.62	0.496±0.12
After 4 Weeks	4±2° C	81.96±1.75	0.846±0.16
	27±2° C	81.82±1.16	1.01±0.24
After 6weeks	4±2° C	81.68±1.58	1.18±0.36
	27±2° C	81.55±1.82	1.34±0.28
After 9 weeks	4±2° C	81.48±1.24	1.42±0.14
	27±2° C	81.32±1.44	1.62±0.12

Conclusions

The prepared ethosomes were spherical and discrete in shape. The size of vesicles was found to be in the range which is desirable for skin penetration. The ethosomes containing 30% w/w ethanol and prepared by sonication method showed highest entrapment efficiency and transdermal flux and can rapidly penetrate through the skin may be because of tiny vesicular size. The pH of the ethosomal gel was compatible with skin, easily spreadable and washable. The in-vitro percentage drug release studies were carried out and the % of drug release was found to be 82.66%. The release mechanism of finasteride from gel was higuchi model (r2, 0.99), suddenly released and continuously releasing. The zeta potential was found to be -39.7 mV which indicates good physical stability. Stability studies carried out for a period of 9 weeks showed negligible changes in the characteristics of ethosomes and further the loss of drug is not more than 4 %. Hence it is concluded that a successful ethosomal gel was formulated for finasteride. Further this can be exploited commercially into a suitable drug formulation.

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